The Cyclization of Parent and Cyclic Hexa-1,3-dien-5-ynes—A Combined Theoretical and Experimental Study

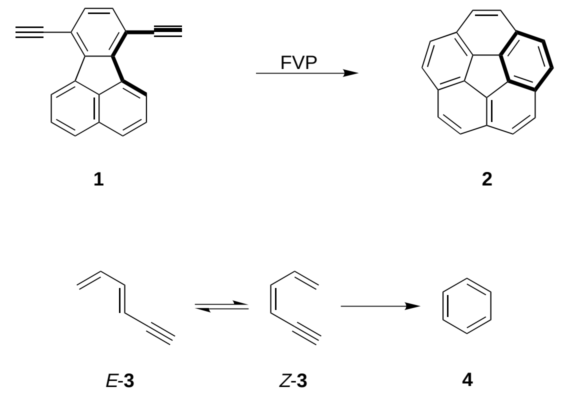
Matthias Prall,[a] Anke Krüger,[b] Peter R. Schreiner,*[a, c] and Henning Hopf*[b]

Abstract: The thermal cycloisomerization of both parent and benzannelated hexa-1,3-dien-5-yne, as well as of carbocyclic 1,3-dien-5-ynes (ring size 7–14), was investigated by using pure density functional theory (DFT) of Becke, Lee, Yang, and Parr (BLYP) in connection with the 6–31G* basis set and the Brueckner doubles coupled-cluster approach [BCCD(T)] with the cc-pVDZ basis set for the parent system. The initial cyclization product is the allenic cyclohexa-1,2,4-triene (isobenzene), while the respective biradical is the transition structure for the enantiomerization of the two allenes. Two consecutive [1,2]-H shifts further transform isobenzene to benzene. For the benzannelated system, the energetics are quite similar and the reaction path is the same with one exception: the intermediate biradical is not a transition state but a minimum which is energetically below isonaphthalene. The cyclization of the carbocyclic 1,3-dien-5-ynes, which follows the same reaction path as the parent system, clearly depends on the ring size. Like the cyclic enediynes, the dienynes were found to cyclize to products with reduced ring strain. This is not possible for the 7- and 8-membered dienynes, as their cyclization products are also highly strained. For 9- to 11-membered carbocycles, all intermediates, transition states, and products lie energetically below the parent system; this indicates a reduced cyclization temperature. All other rings (12- to 14-membered) have higher barriers. Exploratory kinetic experiments on the recently prepared 10- to 14-membered 1,3-dien-5-ynes rings show this tendency, and 10- and 11-membered rings indeed cyclize at lower temperatures.

Keywords: ab initio calculations · cycloaromatization · enynes · isobenzene · macrocycles

Introduction

The thermochemical cyclization of hexa-1,3-dien-5-yne derivatives is of major importance for the synthesis of bowl-shaped molecules like corannulene **2** (Scheme 1)[1–3] and semibuckminsterfullerenes.[4] Examining and understanding the parent reaction in detail will aid in optimizing and extending these synthetic strategies.



Scheme 1. Synthesis of bowl-shaped corannulene **2** from hexa-1,3-dien-5-yne derivative **1**, and the thermal cycloisomerization of **3** to **4**.

In 1969, Hopf and Musso were able to show that hexa-1,3-dien-5-yne **3** undergoes a thermal cycloisomerization to give rise to benzene **4**.[5] The reaction starts above 274 °C, at which point isomerization between *E*-**3** and *Z*-**3** takes place. From a geometrical point of view, *Z*-**3** was believed to be the species which readily cyclizes to **4** (Scheme 1).

As **3** posesses the same number of atoms as **4**, a hydrogen shift or rearrangement has to occur prior to or after

---

[a] Prof. Dr. P. R. Schreiner, Dipl.-Chem. M. Prall
Institut für Organische Chemie, Georg-August-Universität Göttingen
Tammannstrasse 2, 37077 Göttingen (Germany)
E-mail: prs@chem.uga.edu

[b] Prof. Dr. H. Hopf, Dr. A. Krüger
Institut für Organische Chemie
Technischen Universität Braunschweig
Hagenring 30, 38106 Braunschweig (Germany)
Fax: (+49) 531-391-5388
E-mail: h.hopf@tu-bs.de

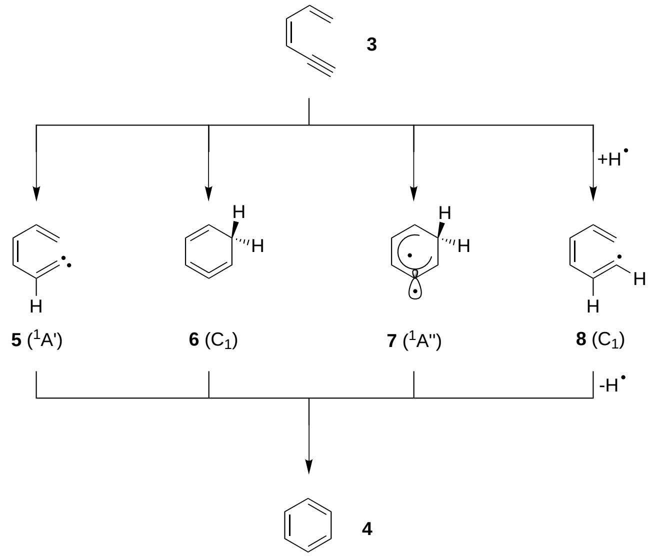
[c] Prof. Dr. P. R. Schreiner
Current address:
Computational Center for Molecular Structure and Design
Department of Chemistry, University of Georgia
Athens, Georgia 30602-2556 (USA)
Fax.: (+1) 706-542-9454

Supporting information for this article is available on the WWW under http://www.wiley-vch.de/home/chemistry/ or from the author.

0947-6539/01/0720-4386 $ 17.50+.50/0

cyclization. Scheme 2 represents the four most likely pathways connecting the structures **3** and **4**:

- [1,2]-H-shift leading to the vinylidene carbene **5** ($^1A'$) and then to **4**.
- thermal cyclization with rearrangement of the π-system giving rise to isobenzene (cyclohexa-1,2,4-triene) **6** which undergoes hydrogen shift to give **4**.
- thermal cyclization to the biradical **7** ($^1A''$) and hydrogen shift to **4**.
- addition of a hydrogen radical (**8**), cyclization, and subsequent loss of $H^\bullet$ to give **4**.

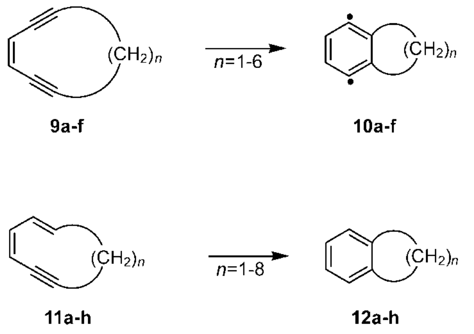


Scheme 2. Possible pathways for the cycloisomerization of **3** to **4**.

Experimental and theoretical studies report that intermediates **6** or **7** are mainly formed during the cyclization at lower temperatures (200–400 °C).[6–8] The role of allene **6** and biradical **7** is, however, unclear.[9, 10] At higher temperatures, processes including the intermediates **5** and **8** are more favorable; this is indicated by the increased formation of pentafulvene as a by-product.[11–15]

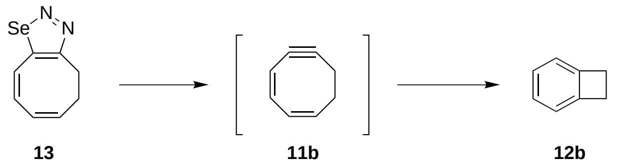
With respect to the formation of fullerene-like moieties or building blocks, the effect of benzannelation on the barriers and enthalpies of formation is also important. Other groups, as well as two of the authors, have shown that the barrier of the corresponding benzannelated enediyne is merely raised, while the reaction enthalpy is ~10 kcal mol^{-1} more endothermic.[16–20] As the cycloisomerization of **3** is apparently not a one-step process, like the Bergman reaction, benzannelation may have a different effect on this reaction.

Another important aspect is the behavior of the dienyne moiety embedded in a carbocyclic system. The structurally similar cyclic enediynes **9a–f** show a correspondence between ring strain and activation enthalpies.[21, 22] In analogy to the Bergman reaction of **9a–f**, at least some of the smaller strained dienyne carbocycles **11a–h** are expected to have lower cyclization barriers (Scheme 3).



Scheme 3. Schematic representation of the enediyne and dienyne carbocycles (**9a–f**, **11a–h**) and their cyclization products (**10a–f**, **12a–h**, respectively).

The synthesis of cycloocta-1,3-dien-5-yne (**11b**) from selenadiazol **13** is a first example for cyclic dienynes.[23, 24] Because of its short lifetime, the highly strained **11b** could only be detected in traces after thermolysis of **13** at 180 °C, but its formation could indirectly be deduced by its cycloisomerization product benzocyclobutene **12b** (Scheme 4). Besides **11b**, the only representative of carbocyclic hexa-1,3-dien-5-ynes ever reported is cyclodeca-1,3-dien-5-yne **11d**; its NMR structural assignment, however, is doubtful.[25, 26] Experimental work on the medium-sized carbocycles **11** still has to be done to characterize this substance class more accurately.

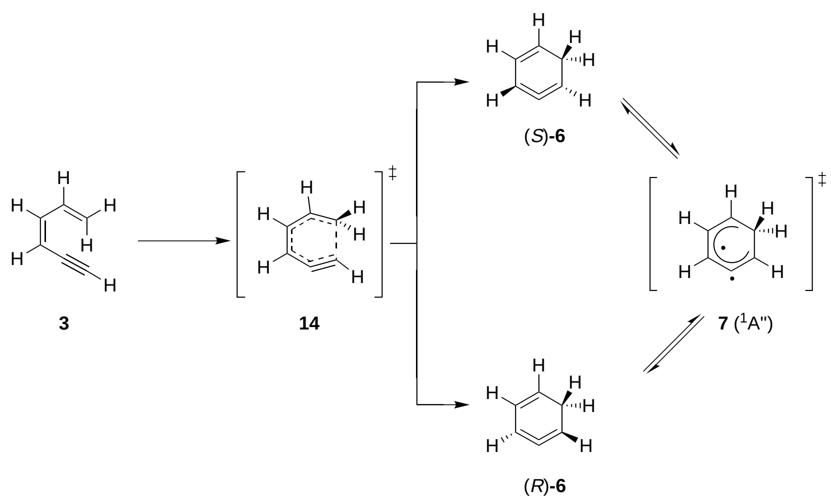


Scheme 4. Synthesis of nonisolable eight membered dienyne **11b** from selenadiazol **13** and cyclization product benzocyclobutene **12b**.

In the present study, the cycloisomerization of the *Z*-hexa-1,3-dien-5-yne parent system **3** to benzene **4** is discussed in detail, including all possible intermediates and transition structures. The computational results are compared with experiment, and conclusions are drawn considering the involvement of isobenzene **6** or biradical **7**. The effect of benzannelation on the cycloisomerization also is investigated, and predictions regarding the energetics for this reaction are made.

In the third part, ring strain effects on the cycloisomerization reaction are discussed theoretically on the basis of the *E*,*Z*-hexa-1,3-dien-5-yne carbocycles **11a–h** and the results are again compared with experimental data.

Computational methods: All calculations were performed with Gaussian98[27] by using Becke's pure gradient-corrected exchange functional[28, 29] and the Lee–Yang–Parr nonlocal correlation functional[30, 31] (BLYP) with a 6–31G*[32] basis set. A restricted approach was used for geometry optimizations, energy evaluations, and frequency analyses of the closed-shell reactants and transition structures, while the biradical structures were computed by an unrestricted broken-spin approach (BS-UBLYP). For the parent and the benzannelated system, additional single-point energies were evaluated by using the Brueckner-doubles (BD) coupled-cluster approach BCCD(T)[33–37] [RBCCD(T) for closed shell, UBCCD(T) for open shell species] and employing Dunning's correlation-consistent valence double-ζ (cc-pVDZ) basis set.[38] All thermal corrections to obtain enthalpy values are taken from BLYP/6–31G* frequency calculations. For comparison of experimental with calculated enthalpies for the parent system, the corrections for these transition states (TSs) were taken from frequency analyses at 623 K (the actual experimental reaction temperature). The use of a larger basis set (6–311+G**) for the key structures of the parent system raised the barriers by only 1–2 kcal mol^{-1}. Although DFT is a single-reference method in the formal sense, it has proven to be quite capable of describing structures with multireference character, such as carbenes[39–44] and biradicals.[21, 22, 45–50] The reasons for this are not entirely clear, but is likely to be due to the fact that the density may be well described by a single configuration in many cases. Hence, this makes the use of DFT for biradicals a case-to-case decision.[20, 47, 51, 52] Based on our and others' recent experience, the choice of functional/basis set combination used in the present work seems, therefore, well justified. We would like to point out that feasible multireference treatments (CASSCF(8,8)/6–31G* and CASMP2(8,8)/6–31G*) are *not* significantly better in describing these types of reactions. For instance, the error in describing the barrier (7–11 kcal mol^{-1}) and reaction enthalpy (2–9 kcal mol^{-1}) for the well-known Bergman cyclization is rather large.[53] Higher-level treatments, such as multireference CI, are currently not feasible.[44]



Scheme 5. Cyclization of dienyne **3** giving rise to isobenzenes (*S*)-**6** and (*R*)-**6**, connected by biradical TS **7**.

Results and Discussion

Parent system: The parent *Z*-hexa-1,3-dien-5-yne, **3**, can cycloisomerize along different paths (Scheme 2); at lower temperatures (200–400 °C), electrocyclic ring closure is favored (via **6** or **7**). Previous work shows that there is a disagreement regarding the intermediate formed along this path. The first experimental reports propose isobenzene structure **6**;[54] an early AM1 study indicated that biradical **7** is not a ground state but rather a transition structure that connects the two enantiomeric isobenzene structures (*S*)-**6** and (*R*)-**6** (C_1 point group).[55] On the basis of the enthalpies of formation, the intermediate was suggested to have biradical structure **7**.[6]

A very detailed B3LYP/6–31G* study has now thrown some light on this dilemma.[56] These computations, which agree nicely with our own BLYP/6–31G* results, show that biradical **7** is indeed a transition structure for the enantiomerization of **6**. Whereas the B3LYP study concentrates on the isomerization of **6** to **4**, our own study combines this issue with the respective chemistry of **3**. The result is that dienyne **3** cyclizes to isobenzene **6**, which racemizes readily via **7** (Scheme 5).

The barrier height between **3** and **6** is 29.2 kcal mol^{-1} at BLYP/6–31G* and 31.7 kcal mol^{-1} at the BCCD(T)/cc-pVDZ level of theory, in good agreement with the experimental result of 30.3 kcal mol^{-1} (Table 1). Experimentally, the formation of the intermediate is 20.4 kcal mol^{-1} endothermic; this correlates best with the value for biradical **7** (BLYP: 18.5 kcal mol^{-1}, BCCD(T): 17.1 kcal mol^{-1}). However, extended computations with a large number of theoretical levels (BLYP,[28, 30, 31] G96LYP,[30, 31, 57] BPW91,[28, 58] HF,[59–61] MP2,[62] and CASSCF(8,8)[63, 64] with a 6–31G* basis set) show that planar **7** *is* a TS (NImag = 1), in which the imaginary vector and IRC calculations indicate movement of the allenic hydrogen atoms out-of-plane toward a twisted allene. Following the path of the dihedral angle of these hydrogens from 0° (**7**) to 98° (**6**) by optimizing the rest of the structure with BLYP/6–31G* and subsequently BCCD(T)/cc-pVDZ single-point calculations show the transition-state nature of **7**

Table 1. Results of the computed enthalpy values for the cycloisomerization of **3** compared with experimental data (all enthalpies in kcal mol^{-1}).

Structure	$\Delta_R H_{298}/\Delta H^{\ddagger}_{623}$ (BLYP/6–31G*)	$\Delta_R H_{298}/\Delta H^{\ddagger}_{623}$ (BCCD(T)/cc-pVDZ)[a]	Experiment[6]
3	0.0	0.0	0.0
14	29.2	31.7	30.3
6	12.6	7.9	20.4
7	18.5	17.1	
17	38.8	38.4	40.5
18	44.1	45.8	
19	57.4	54.6	
20	73.8	75.0	
21	19.8	22.0	–
22	20.6	21.3	–
23	24.2	21.7	–
24	21.5	22.6	–
25	65.3	58.8	–
4	– 65.1	– 67.9	– 64.9

[a] Thermal corrections taken from the BLYP/6–31G* computations.

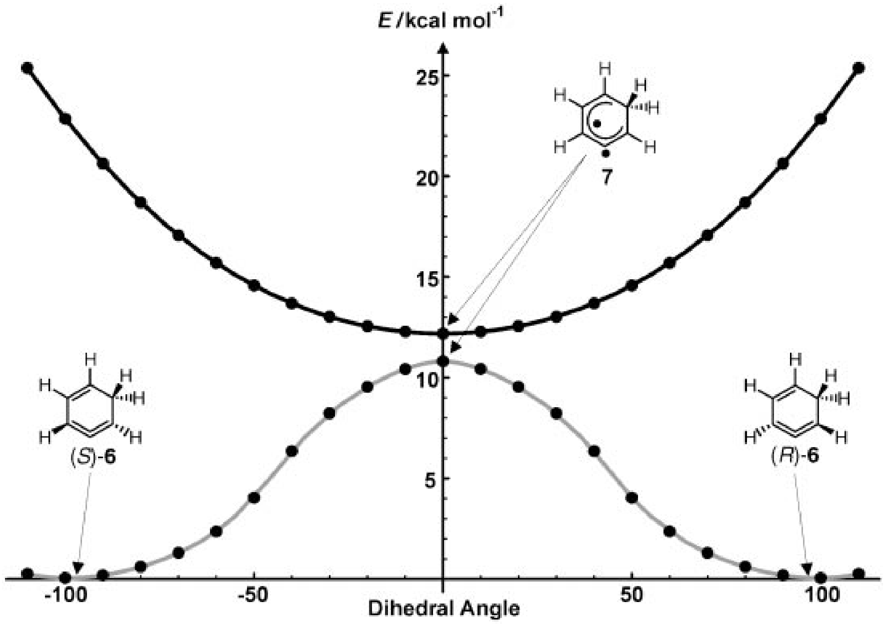


Figure 1. Singlet (bottom) and triplet (top) energy surface of **6** depending on dihedral angle. All points are BCCD(T)/cc-pVDZ//BLYP/6–31G* single-point energies.

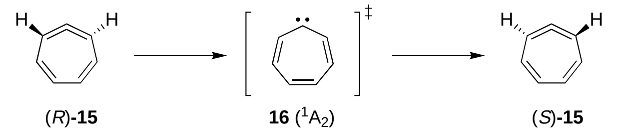
beyond any doubt (Figure 1). The triplet state lies 1.9 kcal mol^{-1} above the open shell singlet and is a true minimum. Additionally, an IRC calculation performed on TS **14** shows the connection between **3** and **6**.

This situation is reminiscent of the enantiomerization of cycloheptatetraene **15** via singlet cycloheptatrienylidene **16** ($^1A_2$, Scheme 6).[65–67] The latter carbene may be considered a one-center biradical, which was long believed to be an intermediate. It is clear now, however, that only the triplet is low-lying and that all low-lying singlets are transition structures.

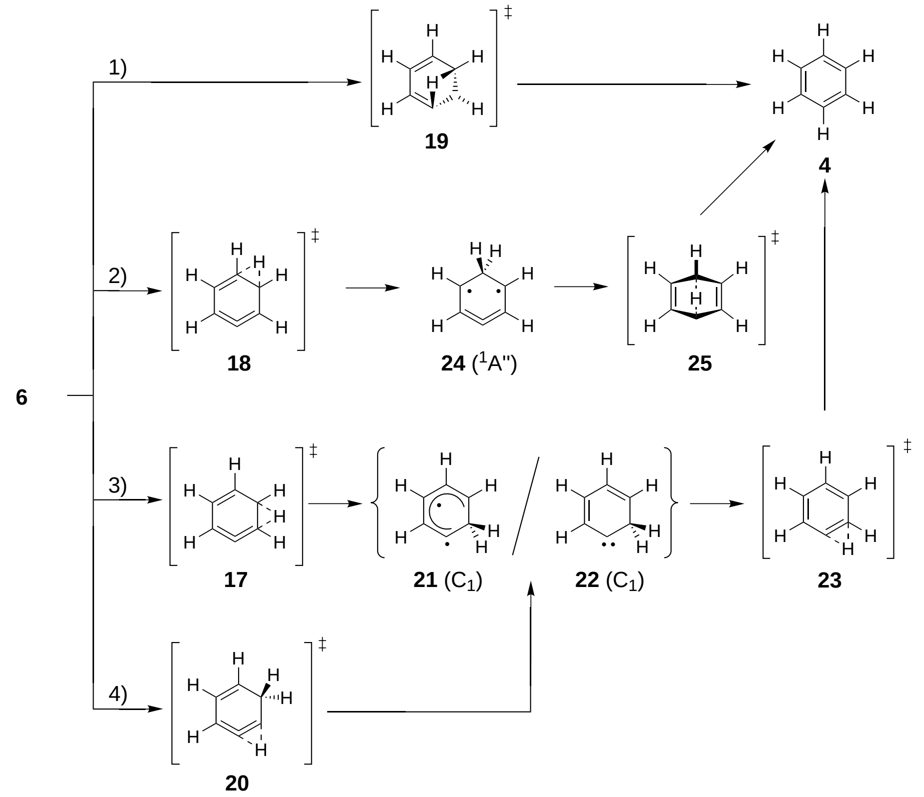
In contrast to previous calculations, we find the biradical TS **7** higher in energy (5.9 kcal mol^{-1} at BLYP or 9.2 kcal mol^{-1} at BCCD(T) above **6** compared with ~2 kcal mol^{-1}); the racemization, however, is still fast.[55, 56] The difference between theory and experiment of about 10 kcal mol^{-1} remains, and more experiments on the cyclization of **3** are needed. For the isomerization of **6** to **4**, different pathways are possible (Scheme 7):

1) direct [1,5] hydrogen shift from the sp^3-hybridized carbon to the allenic carbon via transition structure **19**.
2) [1,2] hydrogen shift from the sp^3-hybridized carbon via TS **18** leading to biradical intermediate **24** and through a subsequent [1,4]-H shift via **25** to **4**.
3) [1,2] hydrogen shift from the sp^3-hybridized carbon via TS **17** to the allenic carbon leading to intermediate **21**/**22** and through a subsequent [1,2]-H shift via **23** to **4**.
4) [1,2] hydrogen shift of the allenic hydrogen via TS **20** giving rise to the same intermediate **21**/**22** and [1,2]-H shift via **23** to **4**.

As noted, path 3 is energetically most favorable. With a barrier of 38.8 kcal mol^{-1} for BLYP or 38.4 kcal mol^{-1} for BCCD(T) above **3**, this path agrees nicely with the experimental result of 40.5 kcal mol^{-1}. The barrier of the perhaps most obvious path, 1, is ~16 kcal mol^{-1} and that of



Scheme 6. Racemization of cycloheptatetraene **15** via planar cycloheptatrienylidene **16**.



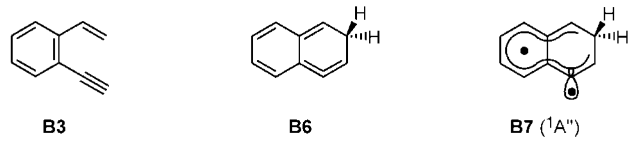
Scheme 7. Possible isomerization paths of isobenzene **6** to benzene **4**.

path 4 more than 34 kcal mol^{-1} higher than for path 3. The first barrier of path 2 is only ~5 kcal mol^{-1} higher than in path 3, but a second barrier of more than 26 kcal mol^{-1} makes this reaction mode likewise unfavorable.

The structure of intermediate **21**/**22** is difficult to characterize. The BLYP energies favor the biradical **21** over the carbenoid structure **22**, while the BCCD(T) data show that **22** is the ground state. Since the difference in energy is within the computational error bars, a clear conclusion cannot be drawn. As the singlet–triplet separation is only 1.9 kcal mol^{-1}, a biradical description of the intermediate seems to be indicated. The intermediate undergoes a second [1,2] hydrogen shift leading to **4**. As the barrier is quite small (BLYP: 4.4 kcal mol^{-1} above **21**, BCCD(T): 0.4 kcal mol^{-1} above **22**) it has not been detected experimentally. The overall experimental exothermicity of the cycloisomerization of **3** to **4** (−64.9 kcal mol^{-1}) again nicely agrees with the BLYP (−65.1 kcal mol^{-1}) and BCCD(T) (−67.9 kcal mol^{-1}) results.

In summary, we could show that **3** undergoes a thermocyclic reaction to one of the enantiomeric isobenzene forms **6**, which are interconnected via biradical TS **7**. Structure **6** isomerizes through two subsequent [1,2]-H shifts to benzene along path 3 via the intermediate **21**/**22**. The comparison between experimental and computational data shows that BLYP/6–31G* and BCCD(T)/cc-pVDZ describe the cycloisomerization of the parent system under consideration quite well; except for the **6**/**7** problem where more computations and experiments are perhaps needed. The time-saving BLYP DFT method does an especially good job, therefore it is sensible to use this method on the large carbocyclic dienynes **11a–h** and their cycloisomerization products, for which the more sophisticated methods are too time-consuming.

Benzannelated system: For the benzannelated system, experimental values are not yet available and, therefore, accurate predictions for the cyclization of **B3** would be useful (Scheme 8). The cyclization barrier (BLYP: 32.1 kcal mol^{-1}, BCCD(T): 36.4 kcal mol^{-1}) is only slightly affected by the benzene ring and lies a little higher in energy than in the parent system. On the other hand, the effect on the cyclization product **B6** or **B7** ($^1A''$) is large. In contrast to the parent system, biradical **B7** is not a TS but a stable structure and lies below the the allenic structure **B6** (2.5 kcal mol^{-1} for BLYP). One explanation may be that the benzylic π-electron of **B7** can delocalize over a larger system, while **B6** loses its aromaticity during cyclization by forming a *o*-quinoide system. Both structures **B6** and **B7** are higher in energy than the parent system.



Scheme 8. Benzannelated dienyne **B3** and cyclization products **B6** and **B7**.

Further isomerization to naphthalene **B4** also occurs through two consecutive [1,2] hydrogen shifts. The barriers of the other two pathways are too high in energy to play a role in the hydrogen transfer. The highest barrier of the two-step shift (BLYP: 44.1 kcal mol^{-1}, BCCD(T): 46.0 kcal mol^{-1}) is 6 kcal mol^{-1} above the respective barrier of the parent system and would require a higher reaction temperature. The intermediate **B21**/**B22** is again a problem (it is a biradical **B21** at BLYP but a carbene at BCCD(T)). The barrier between **B21**/**B22** and **B4** is very low and cannot be determined by a cyclization experiment. The overall exothermicity is a little lower than that of the parent reaction (~60 kcal mol^{-1} vs. ~67 kcal mol^{-1}) because of the aromatic ring already present in **B3**. While **3** gains the full aromatization energy on giving rise to **4**, **B3** only experiences partial aromatization energy on building **B4** from the already aromatic **B3** (Table 2).

Table 2. Results of the computed enthalpy values of the cycloisomerization of **B3** (all enthalpies in kcal mol^{-1}).

Structure	$\Delta_R H_{298}/\Delta H^{\ddagger}_{298}$ (BLYP/6–31G*)	$\Delta_R H_{298}/\Delta H^{\ddagger}_{298}$ (BCCD(T)/cc-pVDZ)[a]
B3	0.0	0.0
B14	32.1	36.4
B6	25.3	25.5
B7	22.8	–[b]
B17	44.1	46.0
B21	20.8	–[b]
B22	21.8	20.7
B23	24.8	22.0
B4	−59.3	−60.1

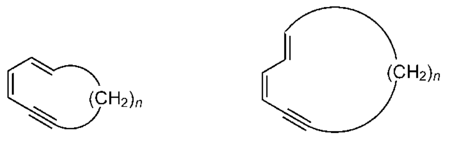
[a] Thermal corrections taken from the BLYP/6–31G* computations. [b] Owing to restricted computer power, the open-shell single points could not be calculated.

Cyclic dienynes: By analogy to enediynes **9a–f**, the cyclic dienynes **11a–h** should be greatly affected by their inherent ring strain. As known experimentally, nine- and ten-membered carbocyclic enediynes **9c** and **9d** readily cyclize at room temperature, while the parent enediyne needs elevated temperatures ($t_{1/2} \approx 1$ h at 155 °C). The reason is the reduction in ring strain by forming the less-strained cyclization product.[18, 21, 22] For similar reasons, the barriers for small cyclic dienynes **11** should decrease and make the molecules cyclize at lower temperatures than parent dienyne **3**.

The following examination deals with the *E*,*Z*-carbocyclic dienynes **11a–h** and their cyclization paths that lead to benzocycloalkenes **12a–h** because the *E*,*Z* species were synthesized and experimentally investigated. Additionally, the structures of *Z*,*Z*-**11a–h** were computed for comparison. While **11a** and **11b** are much more stable in the *Z*,*Z*- than in the *E*,*Z*-conformation (38.2 and 16.1 kcal mol^{-1}, respectively), **11c** and **11d** are only slightly more stable in the *Z*,*Z*-form (7.7 and 2.9 kcal mol^{-1}, respectively). In **11e** both isomers have almost the same energy, while the *E*,*Z*-isomer is preferred by the larger rings **11f–h**.

The *E*,*Z*-isomers **11a–h** can occur in the *cis*- or in the *trans* form (Scheme 9), with a preference for the former by small rings and the latter by large. The cyclization to **26a–h** can, of course, only start from the *cis*-conformer. As calculations on the 14-membered ring **11h** show, the *trans* conformation is only 1.4 kcal mol^{-1} more stable than the *cis*-conformation, and

0947-6539/01/0720-4390 $ 17.50+.50/0

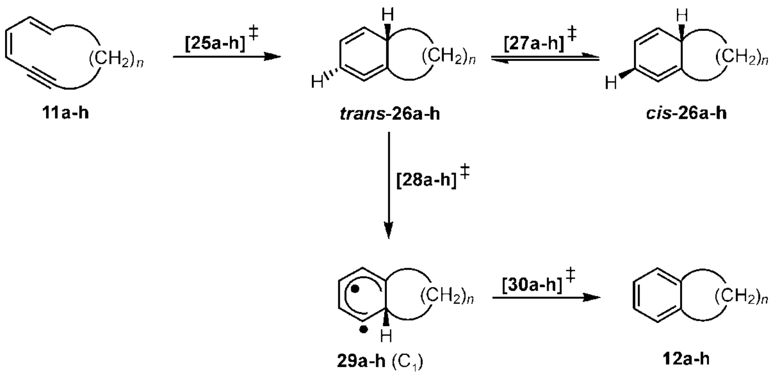


cis-E,Z-**11a-h** *trans-E,Z*-**11a-h**

Scheme 9. Structures **11a–h** in *cis-* and *trans* conformation.

the barrier for interconversion is only 5.6 kcal mol^{-1}. Since **11h** has the most stable *trans* configuration, all other rings either prefer the *cis*-conformation or have lower barriers than **11h**. That is, the *cis/trans* isomerization before the actual cyclization can be neglected kinetically.

In general, the *E,Z*-isomers of **11a–h** initially give rise to the allenes *trans*-**26a–h** via transition structures **25a–h**, while the *Z,Z*-isomers of **11a–h** always lead to *cis*-**26a–h**. The two diastereomeric forms of allenes **26a–h** are connected with each other by biradical TS **27a–h**. The *trans* allenes **26a–h** are then transformed through a [1,2]-H shift to intermediates **29a–h** and through a second [1,2]-H shift further to benzocycloalkenes **12a–h** (Scheme 10). As the second [1,2]-H shift has a much lower barrier than the first one, it is not important kinetically and will therefore only be mentioned in Table 3.



Scheme 10. Cyclization of cyclic dienynes **11a–h**.

Table 3. Results of the computed enthalpy values of the cycloisomerization of **11a–h** [Gibbs free enthalpies (ΔG_{298}) in kcal mol^{-1}].

Ring size	8	9	10	11	12	13	14	Parent
Structure	**b**	**c**	**d**	**e**	**f**	**g**	**h**	System
11	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
25	28.0	20.2	22.9	28.1	37.3	38.6	44.5	32.4
trans-**26**	27.8	14.4	12.1	15.1	20.2	22.4	30.7	14.9
27	–	–	13.8	24.3	33.5	37.5	42.4	21.1
28	37.0	26.7	34.3	39.5	51.4	56.2	62.1	42.7
29	15.9	9.5	14.5	21.4	29.2	34.8	42.6	21.9
30	23.1	13.0	19.4	24.7	37.7	41.3	45.8	28.0
12	−65.8	−76.7	−70.1	−64.8	−49.8	−47.1	−43.7	−62.1

The reactions of seven- and eight-membered dienynes **11a** and **11b** are special cases and have to be considered separately from the other carbocycles. *Trans* allene **26a** cannot be built from **11a** because of the large strain associated with the *trans* configured cyclopropane ring. For the same reason, TS **27a** cannot be reached. As the reaction to **12a** would only be possible from *trans*-**26a** this cyclization is not regarded further. The eight-membered **11b** can, in contrast to **11a**, form a *trans* allene **26b**, it is, however, highly strained as well; this makes the barrier of 28.0 kcal mol^{-1} and an endothermicity of 27.8 kcal mol^{-1} quite reasonable. The barrier for the first [1,2]-H shift is 37.0 kcal mol^{-1}; this makes **11b** a little more reactive than the parent dienyne **3**.

The nine-membered dienyne **11c** has a cyclization barrier of 20.2 kcal mol^{-1}, and the highest H-shift barrier is 26.7 kcal mol^{-1}; this renders **11c** much more reactive than **3**. Only the energy of the allene *trans*-**26c** (14.4 kcal mol^{-1}) is comparable to that of **6** because of the additional ring strain of a *trans* configured five-membered ring in **26c**. The cyclization barrier of ten-membered **11d** (22.9 kcal mol^{-1}) is slightly higher than that of **11c**, while the H-shift barrier is increased to 34.3 kcal mol^{-1}: still well below the barriers of **3**. Allene *trans*-**26d** is not much affected by additional ring strain through the *trans* configuration, and is therefore lower in energy than *trans*-**26c**. With an energy of 12.1 kcal mol^{-1}, *trans*-**26d** is the lowest-lying of allenes **26**. The eleven-membered **11e** has nearly the same energetics as the parent system. With 28.1 and 39.5 kcal mol^{-1} for the cyclization and H-shift barriers, respectively, **11e** is only slightly more reactive than **3**. All remaining cyclic dienynes **11f–h** have higher barriers and energies than the parent system, and are therefore less reactive.

A point worth mentioning is that apart from **11a** and **11b**, which suffer from ring strain in the cyclization products, all barriers and energies *increase* with the enlargement of the ring, so that the potential energy surfaces do not cross each other—except, as already mentioned, *trans*-**26c** (Figure 2).

Experimental Results

As reported elsewhere, two of the authors successfully synthesized a series of cyclo-1,3-dien-5-ynes **11d–h**.[68] These compounds can be obtained in overall yields between 2 and 22% by following a synthetic route with five steps (Scheme 11); they are colorless, volatile liquids, which are stable when stored under argon and cooled.

First experiments on the thermocyclization of **11d–h** have been carried out. The starting materials were heated in o-$C_6D_4Cl_2$, and the thermocyclizations were monitored by ^1H NMR spectroscopy. These first studies clearly showed a correlation between the ring size of the cyclodienyne (and therefore ring strain) and the cyclization temperature. Cyclodeca-1,3-dien-5-yne (**11d**) begins to cyclize at room temperature; as expected the higher homologues require higher cyclization temperatures (Table 4). For cyclotetradeca-1,3-dien-5-yne, **11h**, no cycloaromatization occurred up to 210 °C (b.p. of dichlorobenzene).

Exploratory kinetic experiments of these cyclizations gave preliminary rate constants and activation barriers. The

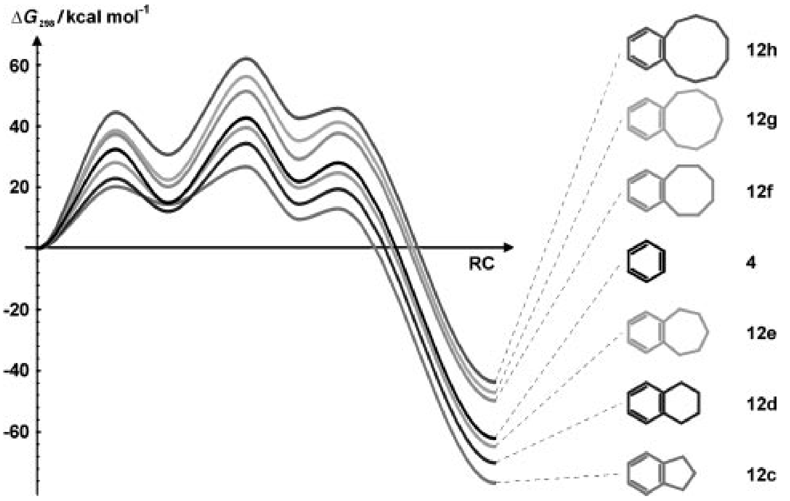


Figure 2. Potential energy surface of the cycloisomerization of **11c–h** to **12c–h** via TSs **26c–h** and **29c–h**.

Table 4. Minimal cyclization temperatures for **11d–h**.

Substance		T_{min} [°C]
Cyclodeca-1,3-dien-5-yne	**11d**	RT
Cycloundeca-1,3-dien-5-yne	**11e**	100
Cyclododeca-1,3-dien-5-yne	**11f**	150
Cyclotrideca-1,3-dien-5-yne	**11g**	traces at 210 °C
Cyclotetradeca-1,3-dien-5-yne	**11h**	no reaction up to 210 °C

measurements were carried out in o-$C_6D_4Cl_2$ and the product/starting material ratio was calculated from the integrated ^1H NMR spectra recorded at different times. Table 5 shows the results obtained; as expected the data are consistent with a first-order reaction (see Figure 3). It is important to note again that the given values represent only approximate results, and that further work has to be done in order to allow a detailed discussion of the experimental results.

Table 5. Results of kinetic experiments for the thermocyclization of **11d–f**.

Substance	$T_{therm.}$ [°C (K)]	10^6 k [s^{-1}]	$\tau_{1/2}$ [h]
11d ($CDCl_3$)	40 (313.15)	7.1 ± 0.3	27.0 ± 1.0
11e (o-$C_6D_4Cl_2$)	165 (438.15)	70 ± 5	2.8 ± 0.2
11f (o-$C_6D_4Cl_2$)	165 (438.15)	3.5 ± 0.1	55.0 ± 1.5

The experimental results agree well with the computed cyclization barriers. On the other hand, all computed [1,2]-shift barriers are apparently too high to allow the formation of benzocycloalkenes at temperatures lower than 200 °C, in contrast to our experimental findings; this problem has not yet been fully solved. One possible explanation is that, in the cyclic system **11a–h**, other hydrogen shifts can occur that are not possible in the parent system **3** because of the absence of the aliphatic chain. In order to give a more satisfactory explanation, additional computational and experimental work on this problem must be carried out.

Conclusion

In the present work we examined the thermal cycloisomerization of parent and benzannelated carbocyclic hexa-1,3-dien-5-ynes by employing a density functional approach and additional coupled-cluster energy single points for the parent system. The applicability of the BLYP DFT functional and of the Brueckner doubles [BCCD(T)] approach is also shown to work well for these systems.

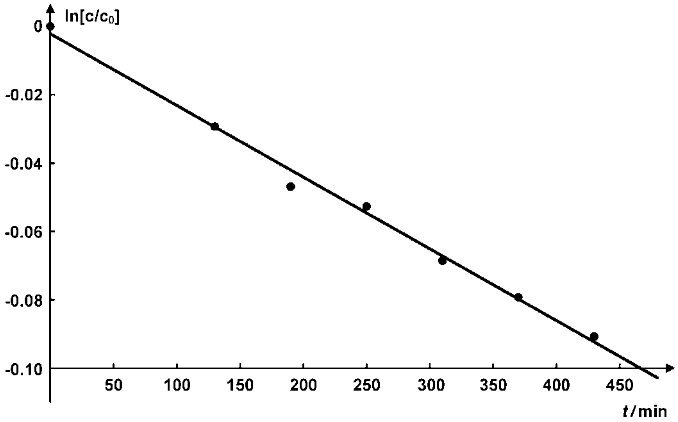
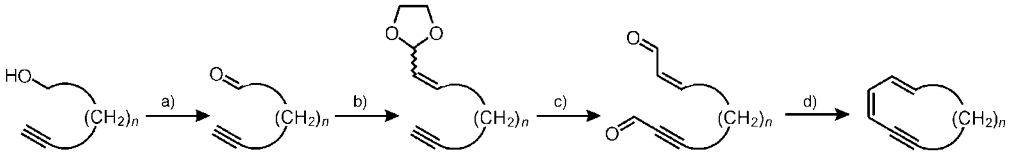


Figure 3. Kinetic diagram of the thermocyclization of **11f**.

For the cycloisomerization of the parent system **3**, both BLYP and BCCD(T) reproduce the experimental values very well. The initial step is a cyclization that forms a six-membered intermediate. It was shown that the formerly proposed biradical intermediate **7** is a transition structure that connects the two enantiomeric isobenzenes **6**, and that **6** is indeed a true intermediate. Two consecutive [1,2]-H shifts transform **6** into benzene **4**; all other shifts, including the direct [1,5]-H shift, have much higher barriers and can be excluded.



11d-h

Scheme 11. Synthesis of cyclo-1,3-dien-5-ynes **11d–h**: a) $(COCl)_2$, DMSO, CH_2Cl_2, NEt_3, −60 °C; b) [1,3]Dioxolan-2-ylmethyltriphenylphosphonium bromide, *t*BuKO, THF, RT; c) *n*BuLi, diethyl ether, −50 °C, DMF, −70 °C, d) $TiCl_3(DME)_{1.5}$, Zn/Cu, DME, reflux.

The benzannelated system **B3** follows a similar reaction pattern to **3**, except that the barriers are a little higher; this should result in a higher cyclization temperature. The overall exothermicity is lower because of the aromatic ring already present in **B3**, and the biradical intermediate **B7** is not a TS but a minimum, which is energetically below isonaphthalene **B6**. One reason for the latter may be that **B6** loses its aromaticity on forming a *o*-quinoide system, while the benzylic π-electron can delocalize over a larger range in **B7**.

To qualitatively understand the effect of ring strain on these reactions, we computed the cyclization energies of carbocyclic 1,3-dien-5-ynes with ring sizes from 7 to 14 carbons (**11a–h**). As was found for the cyclic enediynes, the cycloisomerization of **11** to benzocycloalkenes **12** also clearly depends on the ring size. The small strained rings **11a** and **11b** produce intermediates with even more ring strain and, therefore, **11a** does not cyclize while **11b** has barriers comparable to that of the parent system. The medium rings **11c–e** benefit from inherent ring strain as they produce unstrained intermediates and products; this can be observed in their higher reactivity compared with **3**. With increasing ring size, barriers and endothermicities increase as well. While nine-membered **11c** has the lowest cycloisomerization barriers of all cyclic dienynes **11** (overall barrier: 26.7 kcal mol^{-1}) eleven-membered **11e** is hardly lower in energy than parent **3**. The large rings **11f–h** all have higher barriers and are therefore less reactive than the parent system **3**.

Exploratory kinetic experiments on the recently prepared 10- to 14-membered carbocyclic 1,3-dien-5-ynes **11d–h** support the theoretical findings, as **11d** and **11e** truly cyclize at lower temperatures. However, the rate constants determined indicate lower overall barriers than computed. This problem has not been fully resolved yet. The cyclic systems **11a–h** may undergo other hydrogen shifts which are not possible in parent **3**, as aliphatic substituents are absent. Additional computational and experimental work on this problem will be carried out to give a satisfactory explanation.

Acknowledgments

This work was supported by the Fonds der Chemischen Industrie and the Deutsche Forschungsgemeinschaft. We thank Prof. Dr. A. de Meijere for his support and the RRZN Hannover, as well as the Höchstleistungsrechenzentrum Stuttgart (HLRS) for generous allotments of computer time.

---

[1] L. T. Scott, M. M. Hashemi, D. T. Meyer, H. B. Warren, *J. Am. Chem. Soc.* **1991**, *113*, 7082–7084.

[2] L. T. Scott, P.-C. Cheng, M. M. Hashemi, M. S. Bratcher, D. T. Meyer, H. B. Warren, *J. Am. Chem. Soc.* **1997**, *119*, 10963–10968.

[3] G. Zimmermann, U. Nüchter, S. Hagen, M. Nüchter, *Tetrahedron Lett.* **1994**, *35*, 4747–4750.

[4] P. W. Rabideau, A. H. Abdourazak, H. E. Folsom, Z. Marcinow, A. Sygula, R. Sygula, *J. Am. Chem. Soc.* **1994**, *116*, 7891–7892.

[5] H. Hopf, H. Musso, *Angew. Chem.* **1969**, *81*, 704; *Angew. Chem. Int. Ed. Engl.* **1969**, *8*, 680.

[6] W. R. Roth, H. Hopf, C. Horn, *Chem. Ber.* **1994**, *127*, 1765–1779.

[7] W. R. Roth, H. Hopf, C. Horn, *Chem. Ber.* **1994**, *127*, 1781–1795.

[8] H. Hopf, H. Berger, G. Zimmermann, U. Nüchter, P. G. Jones, I. Dix, *Angew. Chem.* **1997**, *109*, 1236–1238; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1187–1190.

[9] M. Christl, S. Groetsch, *Eur. J. Org. Chem.* **2000**, 1871–1874.

[10] M. Christl, S. Drinkuth, *Eur. J. Org. Chem.* **1998**, 237–241.

[11] G. Zimmermann, M. Nüchter, M. Remmler, M. Findeisen, H. Hopf, L. Ernst, C. Mlynek, *Chem. Ber.* **1994**, *127*, 1747–1753.

[12] U. Nüchter, G. Zimmermann, V. Francke, H. Hopf, *Liebigs Ann./Recueil* **1997**, 1505–1515.

[13] K. Schulz, J. Hofmann, G. Zimmermann, *Liebigs Ann./Recueil* **1997**, 2535–2539.

[14] J. Hofmann, K. Schulz, A. Altmann, M. Findeisen, G. Zimmermann, *Liebigs Ann./Recueil* **1997**, 2541–2548.

[15] G. Zimmermann, *Eur. J. Org. Chem.* **2001**, 457–471.

[16] S. Koseki, Y. Fujimura, M. Hirama, *J. Phys. Chem. A* **1999**, *103*, 7672–7675.

[17] T. Kaneko, M. Takahashi, M. Hirama, *Tetrahedron Lett.* **1999**, *40*, 2015–2018.

[18] W.-H. Chen, N.-Y. Chang, C.-H. Yu, *J. Phys. Chem.* **1998**, *102*, 2584–2593.

[19] W. R. Roth, H. Hopf, T. Wasser, H. Zimmermann, C. Werner, *Liebigs Ann.* **1996**, 1691–1695.

[20] M. Prall, A. Wittkopp, P. R. Schreiner, *J. Phys. Chem.* **2001**, in press.

[21] P. R. Schreiner, *Chem. Commun.* **1998**, *4*, 483–484.

[22] P. R. Schreiner, *J. Am. Chem. Soc.* **1998**, *120*, 4184–4190.

[23] N. Hanold, H. Meier, *Chem. Ber.* **1985**, *118*, 198–209.

[24] H. Meier, N. Hanold, H. Kolshorn, *Angew. Chem.* **1982**, *94*, 67–68; *Angew. Chem. Int. Ed. Engl.* **1982**, *21*, 66–67.

[25] M. Hanack, R. Rieth, *J. Chem. Soc. Chem. Commun.* **1985**, *21*, 1487–1489.

[26] M. Hanack, R. Rieth, *Chem. Ber.* **1987**, *120*, 1659–1666.

[27] *Gaussian 98* (Revision A.7), M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, V. G. Zakrzewski, J. A. Montgomery, R. E. Stratmann, J. C. Burant, S. Dapprich, J. M. Millam, A. D. Daniels, K. N. Kudin, M. C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G. A. Petersson, P. Y. Ayala, Q. Cui, K. Morokuma, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. Cioslowski, J. V. Ortiz, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, C. Gonzalez, M. Challacombe, P. M. W. Gill, B. G. Johnson, W. Chen, M. W. Wong, J. L. Andres, M. Head-Gordon, E. S. Replogle, J. A. Pople, Gaussian, Inc., Pittsburgh PA, **1998**

[28] A. D. Becke, *Phys. Rev. A* **1988**, *38*, 3098–3100.

[29] A. D. Becke, *J. Chem. Phys.* **1993**, *98*, 5648–5652.

[30] B. Miehlich, A. Savin, H. Stoll, H. Preuss, *Chem. Phys. Lett.* **1989**, *157*, 200–216.

[31] C. Lee, W. Yang, R. G. Parr, *Phys. Rev. B* **1988**, *37*, 785–789.

[32] P. C. Hariharan, J. A. Pople, *Theoret. Chimica Acta* **1973**, *28*, 213–222.

[33] K. A. Brueckner, *Phys. Rev.* **1954**, *96*, 508–516.

[34] C. E. Dykstra, *Chem. Phys. Lett.* **1977**, *45*, 466–469.

[35] N. C. Handy, J. A. Pople, M. Head-Gordon, K. Raghavachari, G. W. Trucks, *Chem. Phys. Lett.* **1989**, *164*, 185–192.

[36] K. Raghavachari, G. W. Trucks, J. A. Pople, M. Head-Gordon, *Chem. Phys. Lett.* **1989**, *157*, 479–483.

[37] R. J. Bartlett, J. D. Watts, S. A. Kucharski, J. Noga, *J. Chem. Phys. Lett.* **1989**, *165*, 513–522.

[38] T. H. Dunning, *J. Chem. Phys.* **1989**, *90*, 1007–1023.

[39] H. F. Bettinger, P. v. R. Schleyer, P. R. Schreiner, H. F. Schaefer III in *Computational Analyses of Prototype Carbene Structures and Reactions* (Ed.: E. L. Davidson), World Scientific, Singapore, **1997**, pp. 89–171.

[40] C. J. Cramer, M. A. Hillmyer, *J. Org. Chem.* **1999**, *64*, 4850–4859.

[41] S. E. Worthington, C. J. Cramer, *J. Phys. Org. Chem.* **1997**, *10*, 755–767.

[42] P. G. Wenthold, M. A. Lipton, *J. Am. Chem. Soc.* **2000**, *122*, 9265–9270.

[43] P. G. Wenthold, *J. Chem. Soc. Perkin Trans. 2* **1999**, *11*, 2357–2363.

[44] B. Engels, M. Hanrath, C. Lennartz, *Comput. Chem.* **2001**, *25*, 15–38.

[45] C. J. Cramer, *J. Am. Chem. Soc.* **1998**, *120*, 6261–6269.

[46] J. Gräfenstein, A. M. Hjerpe, E. Kraka, D. Cremer, *J. Phys. Chem. A* **2000**, *104*, 1748–1761.

[47] P. R. Schreiner, M. Prall, *J. Am. Chem. Soc.* **1999**, *121*, 8615–8627.

[48] H. F. Bettinger, P. R. Schreiner, H. F. Schaefer III, P. v. R. Schleyer, *J. Am. Chem. Soc.* **1998**, *120*, 5741–5750.

[49] E. Kraka, D. Cremer, *J. Am. Chem. Soc.* **2000**, *122*, 8245–8264.
[50] G. B. Jones, P. M. Warner, *J. Am. Chem. Soc.* **2001**, *123*, 2134–2145.
[51] W. T. G. Johnson, C. J. Cramer, *J. Am. Chem. Soc.* **2001**, *123*, 923–928.
[52] C. J. Cramer, J. Thompson, *J. Phys. Chem. A* **2001**, *105*, 2091–2098.
[53] J. Hoffner, M. J. Schottelius, D. Feichtinger, P. Chen, *J. Am. Chem. Soc.* **1998**, *120*, 376–385.
[54] M. Christl, M. Braun, G. Müller, *Angew. Chem.* **1992**, *104*, 471–473; *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 473–476.
[55] R. Janoschek, *Angew. Chem.* **1992**, *104*, 473–475; *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 476–478.
[56] A. Navarro-Vázquez, D. Rodríguez, L. Castedo, D. Domínguez, C. Saá, personal communication **2001**.
[57] P. M. W. Gill, *Mol. Phys.* **1996**, *89*, 433–445.
[58] J. P. Perdew, Y. Wang, *Phys. Rev. B* **1992**, *45* (*23*), 13244–13249.
[59] R. McWeeny, G. Dierksen, *J. Chem. Phys.* **1968**, *49*, 4852–4856.
[60] J. A. Pople, R. K. Nesbet, *J. Chem. Phys.* **1954**, *23*, 571–574.
[61] C. C. J. Roothan, *Rev. Mod. Phys.* **1951**, *23*, 69–89.
[62] C. Møller, M. S. Plesset, *Phys. Rev.* **1934**, *46*, 618–622.
[63] R. H. E. Eade, M. A. Robb, *Chem. Phys. Lett.* **1981**, *83*, 362–368.
[64] D. Hegarty, M. A. Robb, *Mol. Phys.* **1979**, *38*, 1795–1812.
[65] P. R. Schreiner, W. L. Karney, P. v. R. Schleyer, W. T. Borden, T. P. Hamilton, H. F. Schaefer III, *J. Org. Chem.* **1996**, *61*, 7030–7039.
[66] M. W. Wong, C. Wentrup, *J. Org. Chem.* **1996**, *61*, 7022–7029.
[67] S. Matzinger, T. Bally, E. V. Patterson, R. J. McMahon, *J. Am. Chem. Soc.* **1996**, *118*, 1535–1542.
[68] H. Hopf, A. Krüger, *Chem. Eur. J.* **2001**, *7*, 4378–4385.

Received: March 12, 2001 [F3122]